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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,289	06/26/2003	Bernhard Lindenthal	SCH-1985	3274

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
09/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/606,289	LINDENTHAL ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,10,12-16 and 19-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10,12-16 and 19-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed June 10, 2009 have been entered. Claims 5, 8, 9, 11, 17, and 18 have been cancelled. Claims 19-25 are added. Claims 1-4, 6, 7, 10, and 12-16 and 19-25 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-11, and 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antagonizing the EP2 receptors by EP2 antagonists recited in the claims, does not reasonably provide enablement for other antagonizing method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. In the instant case, the specification fails to to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to provide information allowing the skilled artisan to ascertain these compounds possessing the recited, and claimed, physiological activity without undue experimentation.

1) the quantity of experimentation necessary,

. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all methods of antagonizing EP2 receptors including, but not limited to, antibodies and gene therapy necessitating an exhaustive search for all embodiments, regardless their chemical formula, immunological properties, or structure, suitable to practice the claimed invention. Examiner notes the claims read on all compounds or modalities possessing the envisioned physiological activity, disclosed, or undisclosed, regardless the modalities desired. Additionally, those antibodies or gene vectors seen as encompassing such physiological activity must be experimentally discovered by the skilled artisan.

2) the amount of direction or guidance provided,

In the instant case, only a limited number of EP2 antagonists examples are set forth, thereby failing to provide sufficient working examples. Those compounds disclosed in the instant specification encompass only a small number of those compound classes envisioned as possessing physiological activity required to practice the invention as herein claimed. Absent that small genus of compounds herein recited, the instant specification is silent as to making, or using, those other compound genera or macromolecules such as proteins, peptides and genes encompassed by the instant claims. Although the specification directs the skilled artisan to specific compounds such as EP2 antagonists, the application is silent with regard to selection of any additional compounds structurally unrelated to those few compounds listed in the instant specification.

3) the presence, or absence, of working examples,

Applicant fails to set forth the criteria that structurally defines, or identifies, those compounds possessing EP2 antagonistic activity. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "EP2 antagonist" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define those structural classes of compounds required to practice the invention as herein claimed, as required by those guidelines set forth in *In re Wands*, supra. Absent exemplification providing guidance as to these compound classes herein envisioned, the instant specification fails to place those compound classes possessing various structural formulas requiring specific

physiological EP2 antagonistic activity in the skilled artisan's possession, absent undue experimentation.

4) the nature of the invention,

The instant invention reading on all possible compounds or modalities possessing the EP2 antagonistic activity envisioned, disclosed, or undisclosed, set forth a broad inventive scope.

5) the state of the prior art,

The instant claims read on all modalities that would antagonize EP2 receptors, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Although various individual compounds possessing the disclosed EP2 receptors activity are known to those of skill in the art, no information is provided to guide the skilled artisan to those diverse genera of structurally divergent compounds possessing similar physiological activity. Examiner is unaware of any nexus, stated in the art, or herein disclosed, attributing the herein envisioned physiological activity to one, or another, structural formula. Simply stated the skilled artisan must employ experimentation to discover compounds possessing these EP2 antagonistic activities required to practice the claimed invention.

6) the relative skill of those in the art

Those individuals skilled in the art possess the required knowledge to perform those assays employed to identify compounds useful for practicing the invention as herein claimed. Applicants' failure to provide adequate guidance as to the envisioned structural formulas employed in the instant claims requires the skilled artisan to

establish, by individual assay, each compound deemed suitable for use in the instant invention.

7) the breadth of the claims.

The instant claims read on all modalities that would antagonize EP2, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Examiner notes the instant claims fail to provide any guidance as to those structural embodiments inherent in those compounds possessing the EP2 antagonistic activity herein envisioned. Applicant's claims encompass every, and all, compounds providing the recited EP2 antagonistic activity regardless the structural formula of such compounds. Absent guidance with regard to the structural identifies of those compounds possessing the recited EP2 antagonistic activity, each compounds must be identified by experimentation in every case. Applicants fail to provide information sufficient to identify the structural formulas of those compounds useful to practice the claimed invention, absent undue experimentation.

Response to Arguments

Applicant's arguments filed June 10, 2009 averring the Examiner's failure to provide evidence challenging the Applicant's statement's of enablement have been fully considered but they are not persuasive. The Applicant apparently relies on the decision in *In re Marzocchi*, 169 USPQ 367,369 (CCPA 1971). However, the examiner notes that The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to

practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."). In the instant case, the burden is met since there is sufficient reasoning set forth in the rejection under 35 USC 112, first paragraph. Specifically, the state of the art, as discussed above, does not provide any nexus between structural modification of a chemical compound and the herein recited physiological effect. The examiner notes that the test of enablement is not whether the Office can provide references teaching away of the instant invention. The eight factors in *In re Wands* are still used for determining whether the specification meets the enablement requirement or not. As discussed above, even with the addition references provided by the applicant in the response, it is still not clear what EP2 antagonists would be able to perform the herein claimed functions since there is no information with regard to the structural-activity relationship being established in the art. At best, we know there are other method to antagonize EP2 receptor. However, the issue at hand is still: there is no information with regard to whether those methods would impaire cumulus

expansion and oocyte maturation or not. There is no adequate working example disclosed. All applicant's remarks are apparently directed to how easy to find or screen a compound to see whether such compounds possessing EP2 antagonistic activity or not. However, it is not the issue here. The issue is not whether how easy or routine to determine a particular compound as EP2 antagonists or not. Again, the issue is that whether the compound can practice the herein claimed method of not without the need to perform undue experimentation. Since the claim is so broad, all the compounds known to man are potential candidates for practicing the instant invention. Therefore, without guidance or working examples, one of skilled in the art would need to perform undue experimentation in order to practice the **full scope** of the herein claimed invention.

Applicant's remarks with regard to working example in pages 8-9 in the response filed June 10, 2009 have been considered, but are not found persuasive. The examiner notes that in the rejection under 35 USC 112, first paragraph, never relies on working example alone to determine whether the specification is enabled or not. When taking all of the factors discussed in *In re Wands* together, the skilled artisan would have to perform undue experimentation to practice the full scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 7, 10, and 12-16 and 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breyer et al. (Annals of the New York Academy of Sciences (2000), 905 (Lysophospholipids and Eicosanoids in Biology and Pathophysiology), 221-231), Narumiya et al. Physiological Review, 1999;79(4):1193-1226, reference of record and Hizaki et al., (Proc. Natl. Acad. Sci. USA, 1999;96:10501-10506) in view of applicant's own admission on page 9, lines 10-21, Norel et al. (British Journal of Pharmacology, 1999;126:867-872) and Noble et al. (American Family Physician, 2000 Jun 15;61(12):3669-76).

Breyer et al. teaches the disruption of EP2 receptors and inhibition of COX-2 can inhibit the ovulation (Examiner notes: oocyte maturation), fertilization and implantation (See page 228 – 229).

Hizaki et al. also teaches the lacking of EP2 receptor in mice may lead to abortive expansion of the cumulus and impaired ovulation (See particularly the abstract and page 10502 – 10505 Results Section).

Nirumiya et al. teaches a general review of EP receptors. Specifically, Nirumiya et al. teaches that the relationship between PGE2 and EP2 receptors in a way that PGE2 interacts with EP2 causing increase in cAMP which in result would induce oophorus maturation (See page 1217, Reproduction section).

The primary references do not expressly teach the use of AH6809 and COX-2 inhibitor such as celecoxib to control fertility or impair cumulus expansion and oocyte maturation.

Applicant's admission on the various prior arts teaching the administration of COX inhibitors such as rofecoxib would disrupt or inhibit the ovulation process and induce delayed follicular rupture.

Norel teaches AH6809 as a EP1/EP2 antagonists (See the abstract).

Noble et al. teaches celecoxib as a COX-2 inhibitor (See the abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to employ AH6809 andr Celecoxib in a method of controlling fertility or impairing cumulus expansion and oocyte maturation.

One of ordinary skill in the art would have been motivated to employ AH6809 and Celecoxib in a method of controlling fertility or impairing cumulus expansion and oocyte maturation. It is known that the inhibition of EP2 activation and COX-2 would lead to impair ovulation, fertilization, implantation, and abortive expansion of cumulus. It is also known that the activation of EP2 receptor would induce oophorus maturation for fertilization. Therefore, employing any known EP2 antagonist, such as AH6809, and any known COX-2 inhibitors, such as celecoxib, to block the activation of EP2 and COX-2 would reasonably expect to lead to the impairment of ovulation, oocyte maturation, implantation, fertilization and abortive expansion of cumulus.

Response to Arguments

Applicant's arguments filed June 10, 2009 averring the presence of the unexpected results, along with the declaration by Dr. Lindenthal and additional evidences in the Exhibit have been considered, but are not found persuasive. The

examiner notes that it is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, although unexpected result are presented when the specific COX-2 inhibitor (Rofecoxib) and EP2 antagonist (ZK6073610) are employed. The instant claims are not commensurate with the scope of the subject matter recited. Therefore, the outstanding rejection under 35 USC 103(a) is still considered as proper.

Applicant's arguments filed June 10, 2009 averring the examiner's hindsight reasoning have been considered, but are not found persuasive. the examiner notes that the cited prior art clearly teaches the lack of or the disruption of EP2 receptor and/or COX-2 inhibition would result in ovulation inhibition (oocyte maturation), impaired ovulation, and abortive expansion of the cumulus. Therefore, possessing the teachings of the cited prior art, one of ordinary skill in the art would be motivated to employ the herein claimed compounds in a method to impair expansion and oocyte maturation.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617

/San-ming Hui/
Primary Examiner, Art Unit 1617